

Review

Clinical review: New technologies – venturing out of the intensive care unit

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Abstract

The delivery of critical care is no longer limited to the intensive care unit. The information gained by utilization of new technologies has proven beneficial in some populations. Research into earlier and more widespread use of these modalities may prove to be of even greater benefit to critically ill patients.

Introduction

Diagnostic and therapeutic interventions done outside the intensive care unit (ICU) are an integral part of the multi-disciplinary continuum of critical care. Presented here is a brief review of hemodynamic monitoring, ancillary studies, and therapeutic modalities that are currently used or that have potential applications in the emergency department (ED).

Esophageal Doppler monitoring

In treating critically ill patients it is often desirable to have available an objective measure of cardiac function and response to therapy. Determinations of cardiac output (CO) have traditionally used a pulmonary artery catheter, employing the thermodilution technique in the operative suite or ICU [1–3]. The risks associated with central venous access, pulmonary arterial injury, embolization, infection, interpretation, and reproducibility were previously addressed and render this modality impractical for use in the ED [2,4,5]. The esophageal Doppler monitor (EDM) can be used to evaluate the velocity and time at which blood travels within the descending aorta using a Doppler signal. EDM-derived variables include peak velocity, flow time, and heart rate. From the EDM-derived variables, CO, stroke volume, and cardiac index can be computed [6–9]. Peak velocity is proportional to contractility and flow time correlates with preload.

Recent reviews in the literature [10–14] support the use of EDM for fluid management in the critically ill both in the operative and ICU settings. Placement of the EDM is similar to insertion of a nasogastric tube, and once it is correctly positioned, with a good Doppler signal acquired, the EDM correlates well with the thermodilution technique and serial measurements can be obtained [15,16]. Reliability of the EDM may be hindered during dysrhythmic states because of the fluctuating or irregular aortic pulse wave. It is clinically useful in distinguishing between a low versus high CO state and determining the response of CO to therapeutic interventions such as an intravenous fluid challenge. Gan and coworkers [10] demonstrated a reduction in length of stay after major surgery using EDM goal-directed fluid management. Case report data support its successful use in guiding therapy in a septic patient [17]. The ease of insertion and interpretation was illustrated in ED studies [18,19], which provide some of the limited evidence for the superiority of EDM data over clinical hemodynamic assessment. EDM may be useful as a tool with which to assess trends in cardiac parameters and clinical response to a given therapy (Table 1). Although outcome data utilizing the EDM are lacking, practical applications in the ED include monitoring intubated patients receiving intravenous inotropic or vasoactive agents. Mechanically ventilated patients often require sedation as part of treatment, and similarly patients being monitored with an EDM may benefit from sedative medications, as delineated in clinical practice guidelines regarding the use of sedation in the ICU [20,21].

Thoracic bioimpedance

Thoracic bioimpedance was initially devised for the space program in the 1960s as a noninvasive means to monitor astronauts during space flight [22]. The science of bioimpedance utilizes differences in tissue impedance that

CO = cardiac output; CRP = C-reactive protein; ED = emergency department; EDM = esophageal Doppler monitor; ICU = intensive care unit; ICG = impedance cardiography; NPPV = noninvasive positive pressure ventilation; PaCO₂ = arterial carbon dioxide tension; PCT = procalcitonin; PetCO₂ = end-tidal carbon dioxide tension; ScvO₂ = central venous oxygen saturation.

occur in response to low levels of electrical current to derive hemodynamic variables. Early work by Nyöber and Kubicek [22,23] derived bioimpedance by means of applying a small current to the thorax and measuring the returning signal coupled to a calculation to derive stroke volume. The currently available technology differs by the choice of two formulae that are currently in use: the earlier mathematical model by Kubicek and the later modification by Sramek-Bernstein, which corrected for certain clinical assumptions made by Kubicek.

Impedance cardiography (ICG) combines bioimpedance over time with the electrocardiographic cycle. The instrument is connected to patients by applying adhesive pads on the neck and/or lateral chest wall areas [8,24]. Patients do not feel the current when the instrument is applied. Studies have shown earlier versions of thoracic bioimpedance to have a correlation coefficient with pulmonary artery catheterization of approximately 0.83 [25]. From the measured values of heart rate, impedance, and electrocardiographic parameters, other hemodynamic parameters are derived, which include cardiac index, CO, stroke index, stroke volume, systemic vascular resistance, and thoracic fluid content. Additional derived data include the pre-ejection period and left ventricular ejection time [24]. The pre-ejection period:left ventricular ejection time ratio reflects contractility [24]. Clinically, ICG has been studied in the management of congestive heart failure [26–28], sepsis [29–31], and trauma [32–35]. In an ED study of patients presenting with shortness of breath [36], application of ICG changed the admitting diagnosis in 5% of patients and accounted for a change in therapy in more than 20%. In applying this technology it should be recognized that its limitations are that data output is derived from calculations, and that continuous electrode contact must be maintained with the skin, which may prove difficult in unstable or diaphoretic patients.

ICG may have a growing role to play in ED management of the critically ill, with further studies delineating the benefit and optimal application of this technique. The use of this technology could be particularly helpful in patients with poor vascular access such as those with peripheral vascular disease and hemodialysis patients (Table 1).

End-tidal carbon dioxide monitoring

End-tidal carbon dioxide refers to the presence of carbon dioxide at the end of expiration (end-tidal carbon dioxide tension [PetCO₂]). Capnometry is the measurement of carbon dioxide gas during ventilation. Capnography refers to the graphical representation of end-tidal carbon dioxide over a period time. The characteristic capnographic waveform is composed of a baseline (representing dead space carbon dioxide), expiratory upstroke, alveolar plateau, end-tidal carbon dioxide, and downstroke. At the peak of the upslope is the PetCO₂ [37]. Depending on the hemodynamic state, the amount of PetCO₂ detected usually correlates with the degree of pulmonary alveolar flow and ventilation [37–39].

Quantitative PetCO₂ is currently measured using a mainstream detector or a sidestream detector utilizing infrared technology. Mainstream detectors are connected to an endotracheal tube for real-time detection of changes in PetCO₂. Sidestream PetCO₂ detectors sample expired gas noninvasively (e.g. in nonintubated patients).

PetCO₂ detection is used as an adjunct to confirm correct endotracheal tube placement [40]. It has also been studied in cardiac arrest as a surrogate of CO and coronary perfusion pressure [41–44]. For victims of cardiac arrest of duration greater than 20 min, capnography readings consistently below 10 mmHg indicate that the chance that there will be no return of spontaneous circulation is nearly 100% [45]. PetCO₂ is useful for managing hemodynamically stable, mechanically ventilated patients. After establishing a gradient between PetCO₂ and arterial carbon dioxide tension (PaCO₂), PetCO₂ can approximate PaCO₂ and serves as a rough guide to ventilatory status [40].

In diabetic ketoacidosis the compensatory response to the metabolic acidosis is an increase in respiratory rate with a concurrent decrease in PaCO₂. Using the relationship between PaCO₂ and PetCO₂, a recent study [46] showed a linear relationship between PetCO₂ and serum bicarbonate with a sensitivity of 0.83 and specificity of 1.0 in patients with diabetic ketoacidosis. PetCO₂ is a helpful noninvasive adjunct for monitoring critically ill patients and for guiding therapy. It potentially can have a more expanded role by providing a quantitative assessment of patients' ventilatory and perfusion status when they present with respiratory failure, metabolic derangements, and post-cardiac arrest (Table 1).

Sublingual carbon dioxide

Recognition of organ-specific sensitivity to decreased flow arose from an understanding of the differences in regional blood flow that occur during systemic hypoperfusion and shock states. Early investigations conducted by Weil and coworkers [47,48] in animals and humans demonstrated an increase in gastric mucosal carbon dioxide during periods of poor perfusion. This led to the concept of gastric tonometry, which is used to measure mucosal carbon dioxide to derive gastric mucosal pH via the Henderson–Hasselbach equation. Experience with this technique demonstrated that it is sensitive and correlates well with other hemodynamic parameters [49]. The time consuming and complex nature of calculating mucosal pH is not practical in the ED; however, it was later discovered that sublingual mucosal carbon dioxide correlates well with the gastric mucosal carbon dioxide [50]. Recent data indicate that the sublingual carbon dioxide–PaCO₂ gradient correlates well with illness severity in septic patients in the ICU [51]. Larger studies evaluating the applicability and response to therapy within the ED setting are needed. Sublingual capnography may serve as a surrogate marker of hypoperfusion. Currently marketed devices for measurement of sublingual carbon dioxide are

Table 1

Normal values (See Appendix 1)

Monitoring tool	Parameter	Normal values	Comments	Patient population in which the parameter is useful
Esophageal Doppler monitor	FTc, PV	FTc: 330–360 ms PV (age-dependent): 20 years 90–120 cm/s; 50 years 70–100 cm/s; 70 years 50–80 cm/s	FTc: correlates with cardiac output, and a mere change in the value in response to a fluid challenge can indicate hypovolemia [10–14] PV: affected by afterload and left ventricular contractility [8]	The hemodynamically compromised Especially useful in patients with contraindications to invasive procedures [17] Mostly studied in intubated, sedated patients
Thoracic bioimpedance	CO/CI, SV/SI, SVR/SVRI, TFC, PEP/LVET	CO correlates well (r = 0.83) with PA catheter [21]	Limited in diaphoretic patients Studies done in CHF, sepsis, trauma, emergency department patients CO correlates well (r = 0.83) with PA catheter [21] PEP/LVET reflect contractility [22–25]	Useful in nonintubated patients – noninvasive
End-tidal carbon dioxide	PetCO ₂	35–45 mmHg >10 mmHg: Critical	Direct correlation (r = 0.64–0.87) [81,82] with PaCO ₂ [37,38] CO and coronary perfusion pressure surrogate [41–44] <10 mmHg indicates unlikely ROSC [45]	COPD Noninvasive ventilation Cardiac arrest
Sublingual capnography [47–49]	SL CAP	70 mmHg [48]	A surrogate for gastric tonometry (i.e. a marker of tissue hypoxia) Shock: >70 mmHg; sensitivity 73%, specificity 100%, positive predictive value 100%	CO ₂ could be an earlier, more rapid indicator of shock than biomarkers ED studies lacking
Lactic acid	LAC	<2.5 mmol/l	>4.0 mmol/l [53]: 98.2% specific for hospital admission from ED; 96% specific in predicting mortality in normotensive inpatients; 87.5% specific in predicting mortality in hypotensive inpatients [55]	Shock of any cause
C-reactive protein	CRP	<50–60 mg/l	Higher CRP level carries worse prognosis [65–67]	Sepsis
Procalcitonin [81]	PCT	0–0.5 ng/ml	>0.6 ng/ml is approximately 69.5% sensitive for infection [84] >2.6 ng/ml: odds ratio 38.3 for septic shock [84]	Infected, septic patients
Central venous oxygen saturation [61,73,74]	Scvo ₂	65–75%	A surrogate for mixed venous oxygen saturation and CI <60% indicates global tissue hypoxia, anemia, sepsis, low CO >80% indicates venous hyperoxia, which implies a defect either in oxygen utilization or delivery [76]	Studies have found Scvo ₂ to be useful in myocardial infarction, intensive care unit, surgical, trauma, and septic/cardiogenic shock patients
Arteriovenous CO ₂ gradient [73]	A–V CO ₂	<5 mmHg	Inversely proportional to CI	Useful for identifying delivery dependent states, and therefore adequacy of tissue perfusion

CHF, congestive heart failure; CI, cardiac index; CO, cardiac output; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; ED, emergency department; FTc, corrected flow time; LVET, left ventricular ejection time; PA, pulmonary artery; PCT, procalcitonin; PEP, pre-ejection period; PetCO₂, end-tidal carbon dioxide tension; PV, peak velocity; SI, stroke index; SL CAP, sublingual capnography; SV, stroke volume; Scvo₂, central venous oxygen saturation; SVR, systemic vascular resistance; SVRI, systemic vascular resistance index; TFC, thoracic fluid content.

rapid and easily applied (see Appendix 1). These devices may be useful in screening for hypoperfused states in ED triage (Table 1).

Point-of-care testing

Point-of-care testing has found its way into the ED. As more rapid bedside analyzers make their way into the marketplace,

health care systems must find the appropriate fit at their institutions. A recent review by Fermann and Suyama [52] addresses the potential applications and pitfalls of their use. A comprehensive review of point-of-care testing will not be revisited here, but rather a few potentially useful biomarkers are discussed.

Lactate

Whole blood analyzers are currently available that allow for measurement of lactate [53]. Lactate is a useful biomarker, providing an indication of tissue hypoperfusion [53–56]. Ability to obtain lactate levels in the ED has significant implications for patient care, and recognition of subclinical hypoperfusion using arterial and venous samples has been shown to correlate well ($r = 0.94$) [57]. Arterial sampling has advantages over venous sampling in hemodynamically compromised patients [58]. Several published studies [57,59–63] have demonstrated the ability of lactate to predict morbidity and mortality even better than base deficit in critically ill patients. Smith and coworkers [59] found that elevated admission blood lactate levels correlated with 24% mortality, and in those whose lactate levels did not normalize within 24 hours the mortality was 82%. The level at which lactate becomes clinically significant may be disputed. Rivers and coworkers [61] used a cutoff of 4 mmol/l to initiate early goal-directed therapy in septic patients. Blow and coworkers [64] aimed for lactate levels of less than 2.5 mmol/l and found that patients in whom this level could not be reached had increased morbidity and mortality (Table 1).

The rate of lactate clearance corresponds to clinical response [63,65]. The goal of resuscitation should therefore be directed not only at normalizing lactate levels but also at doing so in a timely manner, preferably within 24 hours. Lactate measurement in patients with suspected subclinical hypoperfusion served as both an end-point of resuscitation and a means to stratify the severity of illness [62].

C-reactive protein and procalcitonin

Clinical decision making in the ED is often hampered in adult and pediatric patients with possible sepsis because of an imprecise history or a nonlocalizing physical examination. Newer bedside assays may suggest a greater likelihood of infection or severity of illness in the appropriate setting. C-reactive protein (CRP) and procalcitonin (PCT) are two biomarkers that are being investigated in the ED. CRP is a well known acute phase reactant and is a useful marker of inflammation. Its function is to activate complement, opsonize pathogens, and enhance phagocytosis [66]. The physiologic function of PCT is not known. Da Silva and coworkers [67] suggested that CRP might be a more sensitive indicator of sepsis than leukocyte indices alone. Lobo and colleagues [68] found that elevated CRP levels correlated with organ failure and death in an ICU population at admission and at 48 hours. Galetto-Lacour and coworkers [69] evaluated bedside PCT and CRP in a pediatric population and found

the sensitivities for predicting a serious bacterial infection to be 93% and 79%, respectively. In a recent review by Gattas and Cook [70] they suggested that PCT may be useful in excluding sepsis if it is in the normal range (Table 1). Bedside PCT and CRP are currently not approved by the Food and Drug Administration in the USA, but they are on the horizon and may assist with clinical decision-making in the ED setting in patients with suspected sepsis or a serious bacterial infection [71].

Mixed/central venous oximetry and arterial-venous carbon dioxide gradient

Wo and coworkers [72] and Rady and colleagues [73] first described the unreliability of the traditional end-point of normal vital signs in the ED resuscitation of critically ill patients. Rady and coworkers [73] found a persistent deficit in tissue perfusion by demonstrating a decreased central venous oxygen saturation ($ScvO_2$) despite normal vital signs after resuscitation. Increased capillary and venous oxygen extraction leads to a lower $ScvO_2$, which is an indication of increased oxygen consumption or decreased oxygen delivery. Persistently decreased $ScvO_2$ after resuscitation predicts poor prognosis and organ failure [73]. Rivers and coworkers [74] reviewed current evidence comparing mixed venous oxygen saturation and $ScvO_2$; they found that, although a small difference in the absolute saturation value may exist, critically low central venous saturations may still be used to guide therapy. $ScvO_2$ can be measured from blood obtained from a central line inserted into the subclavian or internal jugular vein. Alternatively, newer fiberoptic enabled catheters can provide a real-time display of $ScvO_2$ after initial calibration [73] (Table 1).

Johnson and Weil [75] described the ischemic state seen in circulatory failure as a dual insult of decreased oxygenation and increased tissue carbon dioxide levels. Evidence of carbon dioxide excess was found in cardiac arrest studies demonstrating an elevated arteriovenous carbon dioxide difference [76–78]. In a small observational study [78], derangements in the arteriovenous carbon dioxide gradient were found to exist in lesser degrees of circulatory failure and that this relation correlated inversely with CO. A relationship between mixed venous–arterial carbon dioxide gradient and cardiac index was also observed in a study of septic ICU patients [79]. By measuring $ScvO_2$ or by calculating an arterial central venous carbon dioxide gradient, clinicians can detect subclinical hypoperfusion and have a fair estimate of cardiac function when vital signs do not fully account for a clinical scenario [80]. These modalities can be employed in either an ED or an ICU setting (Table 1).

Therapeutics

Early goal-directed therapy

The combination of early detection of subclinical hypoperfusion and goal-directed therapy in septic patients was advanced by the ED-based protocol devised by Rivers and

coworkers [61]. With early implementation of ScvO₂ monitoring to guide fluid, inotropic, and blood product administration, a significant mortality reduction was observed in patients with severe sepsis and septic shock. The absolute mortality benefit in the treatment group (30.5%) as compared with the control group (46.5%) was 16%. Benefits from early goal-directed intervention were seen as late as 60 days after admission. Efforts to disseminate and apply early goal-directed therapy are underway and multidisciplinary teams may be employed to continue the protocol started in the ED in the ICU. Early identification and treatment of patients at a critical juncture in early sepsis supports the application of this modality in emergency medicine and critical care.

Noninvasive positive pressure ventilation

Noninvasive positive pressure ventilation (NPPV) has been used for a number of years in the ICU and for patients with obstructive sleep apnea. Recently, NPPV has found an increasing role in the ED. Continuous positive airway pressure ventilation may assist patients by improving lung compliance and functional residual capacity [81]. In the ED patients with acute exacerbations of asthma, chronic obstructive pulmonary disease, and congestive heart failure resistant to medical therapy are often intubated for respiratory support. Previously studied indications for employing NPPV in the ED include hypoxic respiratory failure, exacerbation of chronic obstructive pulmonary disease, asthma, and pulmonary edema [81]. In a study into the use of NPPV for patients with congestive heart failure conducted by Nava and coworkers [82], overall outcomes were similar for patients who did not receive NPPV, although a greater improvement in arterial oxygen tension and partial carbon dioxide tension, and a decreased rate of intubations was observed in the NPPV group. In a controversial study of congestive heart failure pitting bilevel positive airway pressure against continuous positive airway pressure [83], a greater rate of myocardial infarction was seen in the bilevel group [83]. Asthma treatment in the ED utilizing bilevel positive airway pressure has yielded improved outcomes [84–86]. The avoidance of endotracheal intubation in patients with reversible disease may have a significant impact on clinical care [83]. NPPV is a viable option for emergency physicians managing patients with COPD, asthma, and pulmonary edema to avoid intubations, and impact morbidity and hospital length of stay.

Conclusions

It has been increasingly recognized that the boundaries of critical illness are extending beyond the ICU. Increasing ED patient volumes compounded by limited ward and ICU bed availability introduce a higher percentage of critically ill patients awaiting ICU admission or transfer. Delays in ancillary testing and implementation of therapy must be avoided. Clinicians must be familiar with newer technologies as they arrive and employ those technologies that will most likely have an impact on clinical care. Earlier recognition and

treatment of critical illness by physicians in multiple disciplines can potentially halt disease progression and have a positive impact on patient outcomes.

Competing interests

The author(s) declare that they have no competing interests.

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Appendix 1

The following is a brief listing of manufacturers of various critical care technologies. This is not an endorsement of any of the listed products or manufacturers. The authors do not have any disclosures or financial interests in any of the listed manufacturers.

Esophageal Doppler monitors:

- CardioQ[®] (www.deltexmedical.com)
- HemoSonic 100[®] (www.hemosonic.com)

Mixed-central venous monitor

- Edwards PreSep[®] Central Venous Oximetry Catheter (Edwards LifeScience; www.edwards.com)

Impedance cardiography

- Bio Z[®] (Impedance Cardiography; www.impedancecardiography.com or www.cdic.com)
- Mindwaretech[®] (www.mindwaretech.com)

End-tidal carbon dioxide:

- DataScope[®] (www.datascope.com)

Point-of-care testing:

- Lactate: YSI 2300 STATplus[®] Whole Blood Analyzer (YSI Life Sciences; www.ysi.com/life/glucose-lactate-analyzer.htm)
- Procalcitonin: PCT LIA[®] (Brahms; www.procalcitonin.com)
- C-reactive protein: Nycocard[®] CRP (Axis-Shield; www.axis-shield-poc.com)